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(54) Title: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO HELICOBACTER PYLORI AND VACCINE COMPOSITIONS THEREOF

(57) Abstract

Recombinant or substantially pure preparations of *H. pylori* polypeptides are described. The nucleic acids encoding the polypeptides also are described. The *H. pylori* polypeptides are useful for diagnostics and vaccine compositions.

NSDOCID: <WO 9818323A1 1 >

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CLAIMS

- 1. An isolated nucleic acid comprising a nucleotide sequence encoding an H. pylori polypeptide at least about 60% homologous to an amino acid sequence 5 selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.
- 2. An isolated nucleic acid comprising a nucleotide sequence encoding an H. pylori polypeptide selected from the group consisting of SEQ ID NO: 74-SEQ ID 10 NO: 146.
 - 3. An isolated nucleic acid which encodes an H. pylori polypeptide, comprising a nucleotide sequence at least about 60% homologous to a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.
 - The isolated nucleic acid of claim 1, comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.
 - An isolated nucleic acid molecule encoding an H. pylori polypeptide, 5. comprising a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule comprising the nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.
 - 6. An isolated nucleic acid comprising a nucleotide sequence of at least 8 nucleotides in length, wherein the sequence hybridizes under stringent hybridization conditions to a nucleic acid having a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.
- An isolated nucleic acid comprising a nucleotide sequence encoding an 7. H. pylori cell envelope polypeptide or a fragment thereof, said nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, SEQ ID NO: 48, SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID 35 NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID

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NO: 11, SEQ ID NO: 71, SEQ ID NO: 17, SEQ ID NO: 57, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, and SEQ ID NO: 21, or a complement thereof.

- 8. The isolated nucleic acid of claim 7, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, and SEQ ID NO: 48, or a complement thereof.
- The isolated nucleic acid of claim 7, wherein said *H. pylori* cell envelope
 polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, and SEQ ID NO: 71, or a complement thereof.
 - 10. The isolated nucleic acid of claim 9, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11 and SEQ ID NO:71, or a complement thereof.
- The isolated nucleic acid of claim 9, wherein said H. pylori outer membrane polypeptide or a fragment thereof is an H. pylori polypeptide having a terminal phenylalanine residue or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, or a complement thereof.
- 12. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cell envelope polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, SEQ ID NO: 121, SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO:

101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, SEQ ID NO: 130, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, and SEQ ID NO: 94.

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13. The isolated nucleic acid of claim 12, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, and SEQ ID NO: 121.

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14. The isolated nucleic acid of claim 12, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, and SEQ ID NO: 130.

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15. The isolated nucleic acid of claim 14, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof selected from the group consisting of SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, and SEQ ID NO: 84 and SEQ ID NO:144.

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- 16. The isolated nucleic acid of claim 14, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, and SEQ ID NO: 131.
- 17. An isolated nucleic acid comprising a nucleotide sequence encoding an H. pylori secreted polypeptide or a fragment thereof, said nucleic acid selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 32, SEQ ID NO: 51, SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 22, SEQ ID NO: 29, SEQ

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ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 53, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, and SEQ ID NO: 68, or a complement thereof.

- An isolated nucleic acid comprising a nucleotide sequence encoding an H. pylori secreted polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 145, SEQ ID NO: 105, SEQ ID NO: 124, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 82, SEQ ID NO: 86, SEQ ID NO: 95, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 122, SEQ ID NO: 126, SEQ ID NO: 132, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, and SEQ ID NO: 141.
- An isolated nucleic acid comprising a nucleotide sequence encoding an H. pylori cellular polypeptide or a fragment thereof, said nucleic acid selected from the group consisting of SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 47, SEQ ID NO: 50,
 SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 69, SEQ ID NO: 70, and SEQ ID NO: 73, or a complement thereof.
 - 20. An isolated nucleic acid comprising a nucleotide sequence encoding an *H. pylori* cellular polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 85, SEQ ID NO: 88, SEQ ID NO: 93, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 120, SEQ ID NO: 123, SEQ ID NO: 133, SEQ ID NO: 137, SEQ ID NO: 142, SEQ ID NO: 143, and SEQ ID NO: 146.
- 21. A probe comprising a nucleotide sequence consisting of at least 8

 nucleotides of a nucleotide sequence selected from the group consisting of SEQ ID NO:

 1-SEQ ID NO: 73, or a complement thereof.
- 22. A recombinant expression vector comprising the nucleic acid of any of claims 1, 2, 3, 4, 5, 6, 7, 12, 17, 18, 19 or 20 operably linked to a transcription regulatory element.

- 23. A cell comprising a recombinant expression vector of claim 22.
- 24. A method for producing an *H. pylori* polypeptide comprising culturing a cell of claim 23 under conditions that permit expression of the polypeptide.

- 25. The method of claim 24, further comprising purifying the polypeptide from the cell.
- 26. A method for detecting the presence of a *Helicobacter* nucleic acid in a sample comprising:
 - (a) contacting a sample with a nucleic acid of any of claims 6 or 21 so that a hybrid can form between the probe and a *Helicobacter* nucleic acid in the sample; and
- (b) detecting the hybrid formed in step (a), wherein detection of a hybrid indicates the presence of a *Helicobacter* nucleic acid in the sample.
 - 27. An isolated *H. pylori* polypeptide comprising an amino acid sequence at least about 60% homologous to an *H. pylori* polypeptide selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.

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- 28. An isolated *H. pylori* polypeptide which is encoded by a nucleic acid comprising a nucleotide sequence at least about 60% homologous to a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73.
- 25 29. The isolated *H. pylori* polypeptide of claim 28, wherein said polypeptide is encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73.
- 30. An isolated *H. pylori* polypeptide which is encoded by a nucleic acid which hybridizes under stringent hybridization conditions to a nucleic acid selected from the group consisting of SEQ ID NO: 1-SEQ ID NO: 73, or a complement thereof.
 - 31. An isolated *H. pylori* polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146.
 - 32. An isolated *H. pylori* cell envelope polypeptide or a fragment thereof, wherein said polypeptide is selected from the group consisting of SEQ ID NO: 76, SEQ

ID NO: 98, SEQ ID NO: 121, SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, SEQ ID NO: 130, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 81, and SEQ ID NO: 94.

- 33. The isolated polypeptide of claim 32, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 76, SEQ ID NO: 98, and SEQ ID NO: 121.
- 34. The isolated polypeptide of claim 32, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 83, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, SEQ ID NO: 84, SEQ ID NO: 144, SEQ ID NO: 90, and SEQ ID NO: 130.
 - 35. The isolated polypeptide of claim 34, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof selected from the group consisting of SEQ ID NO: 74, SEQ ID NO: 115, SEQ ID NO: 87, SEQ ID NO: 116, and SEQ ID NO: 84 and SEQ ID NO:144.
- 36. The isolated polypeptide of claim 34, wherein said *H. pylori* outer
 30 membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof selected from the group consisting of SEQ ID NO: 89, SEQ ID NO: 118, SEQ ID NO: 108, SEQ ID NO: 110, SEQ ID NO: 80, SEQ ID NO: 112, SEQ ID NO: 128, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 101, SEQ ID NO: 103, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, and SEQ ID NO: 131.

An isolated *H. pylori* cell envelope polypeptide or a fragment thereof, wherein said polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, SEQ ID NO: 48, SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, SEQ ID NO: 71, SEQ ID NO: 17, SEQ ID NO: 57, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, and SEQ ID NO: 21.

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38. The isolated polypeptide of claim 37, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* inner membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 25, and SEQ ID NO: 48.

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39. The isolated polypeptide of claim 37, wherein said *H. pylori* cell envelope polypeptide or a fragment thereof is an *H. pylori* outer membrane polypeptide or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 10, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11, and SEQ ID NO: 71.

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40. The isolated polypeptide of claim 39, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue and a C-terminal tyrosine cluster or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 42, SEQ ID NO: 14, SEQ ID NO: 43, SEQ ID NO: 11 and SEQ ID NO:71.

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41. The isolated polypeptide of claim 39, wherein said *H. pylori* outer membrane polypeptide or a fragment thereof is an *H. pylori* polypeptide having a terminal phenylalanine residue or a fragment thereof encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 45, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 7, SEQ ID NO: 39, SEQ ID NO: 55, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 52, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 58.

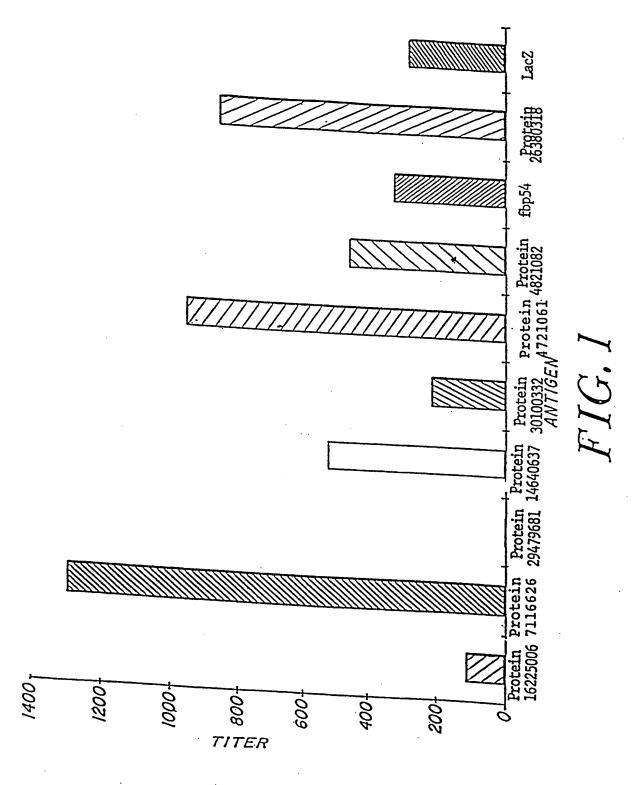
- 42. An isolated *H. pylori* cellular polypeptide or a fragment thereof, wherein said polypeptide is selected from the group consisting of SEQ ID NO: 85, SEQ ID NO: 88, SEQ ID NO: 93, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO: 120, SEQ ID NO: 123, SEQ ID NO: 133, SEQ ID NO: 137, SEQ ID NO: 142, SEQ ID NO: 143, and SEQ ID NO: 146.
- 43. An isolated *H. pylori* cellular polypeptide or a fragment thereof, wherein said polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ
 10 ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 47, SEQ ID NO: 50, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 69, SEQ ID NO: 70, and SEQ ID NO: 73.
- 44. An isolated *H. pylori* secreted polypeptide or a fragment thereof, wherein said polypeptide is selected from the group consisting of SEQ ID NO: 145, SEQ ID NO: 105, SEQ ID NO: 124, SEQ ID NO: 75, SEQ ID NO: 77, SEQ ID NO: 82, SEQ ID NO: 86, SEQ ID NO: 95, SEQ ID NO: 102, SEQ ID NO: 104, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 122, SEQ ID NO: 126, SEQ ID NO: 132, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 140, and SEQ ID NO: 141.
- 45. An isolated *H. pylori* secreted polypeptide or a fragment thereof, wherein said polypeptide is encoded by a nucleic acid selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 32, SEQ ID NO: 51, SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 22, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 44, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 53, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, and SEQ ID NO: 68.
 - 46. A fusion protein comprising an *H. pylori* polypeptide which comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146 operatively linked to a non-*H. pylori* polypeptide.

- 47. A vaccine formulation for prophylaxis or treatment of an *H. pylori* infection comprising an effective amount of at least one isolated nucleic acid of any of claims 1, 2, 3, 4, 5, 6, 7, 12, 17, 18, 19, or 20.
- 48. A vaccine formulation for prophylaxis or treatment of an *H. pylori* infection comprising an effective amount of at least one *H. pylori* polypeptide or a fragment thereof of any of claims 26, 27, 28, 29, 30, 31, 32, 37, 42, 43, 44 or 45.
- 49. A vaccine formulation of claim 47, further comprising a pharmaceutically acceptable carrier.
 - 50. A vaccine formulation of claim 48, further comprising a pharmaceutically acceptable carrier.
- 15 51. A vaccine formulation of claim 49, wherein the pharmaceutically acceptable carrier comprises an adjuvant.
 - 52. A vaccine formulation of claim 50, wherein the pharmaceutically acceptable carrier comprises an adjuvant.
 - 53. A vaccine formulation of claim 49, wherein the pharmaceutically acceptable carrier comprises a delivery system.
- 54. A vaccine formulation of claim 50, wherein the pharmaceutically acceptable carrier comprises a delivery system.
 - 55. A vaccine formulation of claim 53, wherein the delivery system comprises a live vector.
- 30 56. A vaccine formulation of claim 54, wherein the delivery system comprises a live vector.
 - 57. A vaccine formulation of claim 55, wherein the live vector is a bacteria or a virus.
 - 58. A vaccine formulation of claim 56, wherein the live vector is a bacteria or a virus.

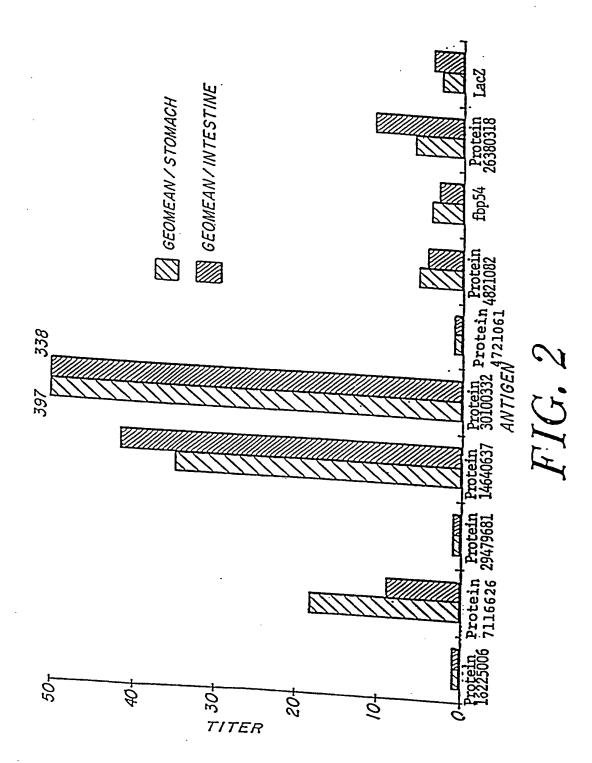
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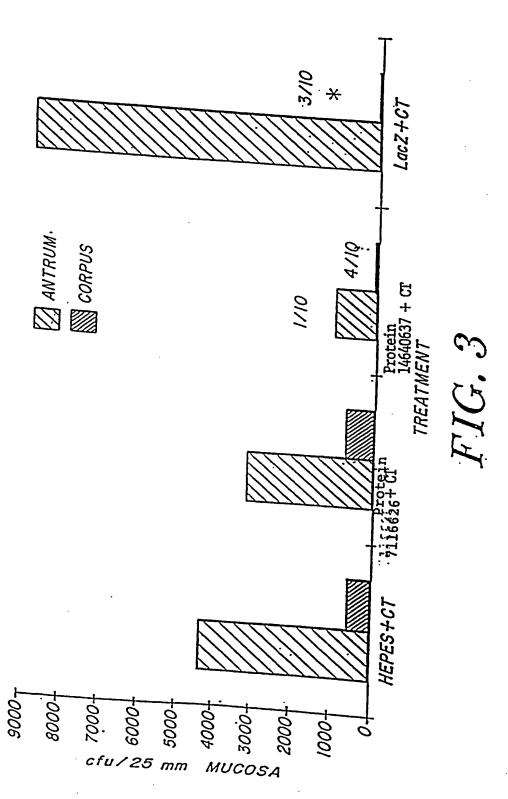
- 59. A vaccine formulation of claim 53, wherein the pharmaceutically acceptable carrier further comprises an adjuvant.
- 5 60. A vaccine formulation of claim 54, wherein the pharmaceutically acceptable carrier further comprises an adjuvant.
 - 61. A method of treating or reducing a risk of *H. pylori* infection in a subject comprising administering to a subject a vaccine formulation of claim 47, such that treatment or reduction of risk of *H. pylori* infection occurs.
 - 62. A method of treating or reducing a risk of *H. pylori* infection in a subject comprising administering to a subject a vaccine formulation of claim 48, such that treatment or reduction of risk of *H. pylori* infection occurs.
 - 63. A method of producing a vaccine formulation comprising: combining at least one isolated *H. pylori* polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146 with a pharmaceutically acceptable carrier to thereby form a vaccine formulation.
 - 64. A method of producing a vaccine formulation comprising:
 - (a) providing at least one isolated *H. pylori* polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146; and
- (b) combining at least one said isolated *H. pylori* polypeptide or a fragment thereof with a pharmaceutically acceptable carrier to thereby form a vaccine formulation.
 - 65. A method of producing a vaccine formulation comprising:
- (a) culturing a cell under condition that permit expression of an *H*.

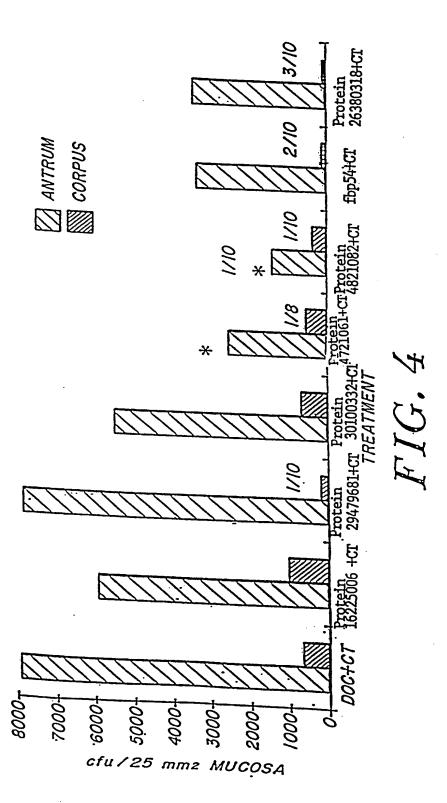
 30 pylori polypeptide or a fragment thereof selected from the group consisting of SEQ ID NO: 74-SEQ ID NO: 146;
 - (b) isolating said *H. pylori* polypetide from said cell; and
- (c) combining at least one said isolated *H. pylori* polypeptide or a fragment thereof with a pharmaceutically acceptable carrier to thereby form a vaccine formulation.



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74	
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•	MARULMKKFVALGLLSAVLSSSLLAEGDGVYIGTNYQLGDARLNSNIYNTGDCTGS
	* * . *
74	BLOCK B BLOCK C
115	SDWRIGH-DLYGINERI CETTOERA
87	SDWRHGN-DLTGI.NFKI.GEV.CEN.N.
116	SURQATNATIKGFDALLGYOFFER
84	VVGCPPGLTANKHNPGGTNIMJESVANON GEFDALLGYQFFFEKHFGLRL
	VVGCPPGLTANKHNPGGTNINWHSKYANGALUGFGLNVGYKKFFQFKSLDMTSKWFGFRV
	* * * * * * * * * * * * * * * * * * * *
74	VODY
115	YGFLDWFNTSGTEHTKTNLLTYGGGGD
87	YGFLUWFNTSGTEHTKTNLLTYGGGGD YGFFUYAHANSIKLKNPNYNSEAAOWAGGT
116	
84	YGFFIYAHANSIKLKNPNYNSEAAQVASQILGKQEINRLTNIADPRTFEPNMLTYGGAMD YGLFIYGHADLGKQVY
	YGLFTYGHADLGKQVYAPNKIQLDMVSWGVGSD
	BLOCK D
74	LIVNLIPLDKFAIGLICGUOLAGUEL
115	LIVNLIPLDKFALGLIGGVQLAGNTWMFPYDVNQLIVNLIPLDKFALGLIGGVQLAGNTWMFPYDVNQ
87	LIVNLIPLDKFALGLIGGVQLAGNTWMFPYDVNQVMVNVINNGIMSLGAFGGIOLAGNGULVAGNGU
116	
84	VMVNVINNGIMSLGAFGGIQLAGNSWLMATPSFEGILVEQALV LLADIIDKDNASFGIFGGVAIGGNTWKSSAAART
* :	LLADIIDKDNASFGIFGGVAIGGNTWKSSAANYWKEQIIEAKGPDVCTPTYCNPNAPYST
	BLOCK E
74	TRFOFLWNLGGRMRVGDRSAEDAGWNDSBLOCK F
115	TRFQFLWNLGGRMRVGDRSAFEAGVKFPMVNQGSKDVGLIRYYSWYV SKKATSFQFLFNVGARLRILKHSSTFAGUKERWY
87	SKKATSFQFLFNVGARLRILKHSSTFAGUERDVALLERYYSWYV
116	SKKATSFQFLFNVGARLRILKHSSIEAGVKFPMLKKNPYITSKDVGLIRYYSWYV SKKATSFQFLFNVGARLRILKHSSIEAGVKFPMLKKNPYITAKNLDIGFRRVYSWYV
84	SKKATSFQFLFNVGARLRILKHSSIEAGVKFPMLKKNPYITAKNLDIGFRVYSWYV NTSTVAFQVWLNFGVRANIYKHNGVERCYBYDI
	NTSTVAFQVWLNFGVRANIYKHNGVEFGVRVPLLINKFLSAGPNATNLYYHLKRDYSLYL
	* ** *.
74	DYVFTF
115	DYVFTF
87	NYVFTF
116	NYVFTF
84	GYNYTF
	* .**
•	

FIGURE 5

aaSeq	ID#
83 89	MRKLFIPLLLFSALEANEKNGFFIEAGFETGLLEGTQTQEKRHTTTKNTYATYNYLPTDT
108	
118	MRKLFIPLLFSALEANEKNGFFIEAGFETGLLEGTQTQEKRHTTTKNTYATYNYLPTDT MRKLFIPLLLFSALEANEKNGFFIEAGFETGLLEGTQTQEKRHTTTKNTYATYNYLPTDT
83 89	ILKRAANLFTNAEAISKLKFSSLSPVRVLYMYNGQLTIENFLPYNLNNVKLSFTDAQGNV
108	Try and a second
118	ILKRAANLFTNAEAISKLKFSSLSPVRVLYMYNGQLTIENFLPYNLNNVKLSFTDAQGNT ILKRAANLFTNAEAISKLKFSSLSPVRVLYMYNGQLTIENFLPYNLNNVKLSFTDAQGNV
83	IDLGVIETIDKUSVIJA RODUMA
89	IDLGVIETIPKHSKIVLPGEAFDSLKIDPYTLFLPKIEATSTSISDANTQRVFET
108	
118	IDLGVIETIPKHSKIVLPGEAFDSLKEAFDKIDPYTLPLPKFEATSTSISDTNTQRVFET IDLGVIETIPKHSKIVLPGEAFDSLKIDPYTLFLPKIEATSTSISDANTQRVFET
83	LNKIKTNLVVNYRNEN
89	LNKIKTNLVVNYRNENKFKDHENHWEAFTPQTAEEFTNLMLNMIAVLDS
108	
118	LNNIKTNLIMKYSNENPNNFNTCPYNNNGNTKNDCWQNFTPOTAEEFTNLMLNMIAVLDS LNKIKTNLVVNYRNENKFKDHENHWEAFTPQTAEEFTNLMLNMIAVLDS
83	QSWGDAILNAPEFFTNSDTDCD
89	QSWGDAILNAPFEFTNSPTDCDNDPSKCVNPGTNGLVNSKVDQKYVLNKQDIVNKFKNKA
108	
118	QSWGDAILNAPFEFTNSSTDCDSDPSKCVNPGVNGRVDTKVDQQYILNKQGIINNFRKKI QSWGDAILNAPFEFTNSPTDCDNDPSKCVNPGTNGLVNSKVDQKYVLNKQDIVNKFKNKA
83	
89	DLDVIVLKDSGVVGLGSDITPSNNDDGKHYGQLGVVASALDPKKLFGDNLKTINLEDLRT
108	
118	
	DLDVIVLKDSGVVGLGSDITPSNNDDGKHYGQLGVVASALDPKKLFGNDLKTINLEDLRT
83	TI UEBOURVOITE
89	ILHEFSHTKGYGHNGNMTYQRVPVTKDGQVEKDSNGKPKDSDGLPYNVCILHEFSHTKGYGHNCDMTTKONYTT
108	THE PROPERTY OF THE PROPERTY O
118	ILHEFSHTKGYGHNGNMTYQRVPVTKDGQVEKDSNGKPKDSDGLPYNVCSLYGGSNQPAF ILHEFSHTKGYGHNGNMTYORVPUTKDCQVEKDSNGKPKDSDGLPYNVCSLYGGSNQPAF
110	ILHEFSHTKGYGHNGNMTYQRVPVTKDGQVEKDSNGKPKDSDGLPYNVCSLYGGSNQPAF
83	
89	PSNYPNSTVHNCADURACELORIS
108	PSNYPNSIYHNCADVPAGFLGVTAAVWQQLINQNALPINYANLGSQTNYNLNASLNTQDL PSNYPNSIYHNCADVPAGFLGVTANUNOOLINON
118	PSNYPNSIYHNCADVPAGFLGVTAAVWQQLINQNALPINYANLGSQTNYNLNASLNTQDL PSNYPNSIYHNCADVPAGFLGVTAAVWQQLINQNALPINYANLGSQTNYNLNASLNTQDL

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FIGURE 6 (Cont'd)

SMLSTIQKTEVTSSVTNHHFSNASQS SMLSTIQKTEVTSSVTNHHFSNASQS SMLSTIQKTEVTSSVTNHHFSNASQS	AKAVNQKVQQLSYGGGIDLLLDFITT NKAVNQKVQQLSYGGGIDLLLDFITT AKAVNQKVQQLSYGGGIDLLLDFITT ***********************************	JLNKVKGSGNLDVATGLNYRYKHSKYS JLNKVKGSGNLDVATGLNYRYKHSKYS JLNKVKGSGNLDVATGLNYRYKHSKYS	SHFKVFFNYGGCF SHFKVFFNYGWF
ANSMLSTIQKTEVTSSVTNHHFSNASQSERSPILGVNAKIGYQNYFNDFIGLAYYGIIKY ANSMLSTIQKTEVTSSVTNHHFSNASQSFRSPILGVNAKIGYQNYFNDFIGLAYYGIIKY ANSMLSTIQKTEVTSSVTNHHFSNASQSFRSPILGVNAKIGYQNYFNDFIGLAYYGIIKY	NYAKAVNQKVQQLSYGGIDLLLDFITTYSNKNSPTGIQTKRNFSSSFGIFGGLRGLYNS NYAKAVNQKVQQLSYGGGIDLLLDFITTYSNKNSPTGIQTKRNFSSSFGIFGGLRGLYNS NYAKAVNQKVQQLSYGGGIDLLLDFITTYSNKNSPTGIQTKRNFSSSFGIFGGLRGLYNS	YYVLNKVKGSGNLDVATGLNYRYKHSKYSVGISIPLIQRKASVVSSGGDYTNSFVFNEGA YYVLNKVKGSGNLDVATGLNYRYKHSKYSVGISIPLIQRKASVVSSGGDYTNSFVFNEGA YYVLNKVKGSGNLDVATGLNYRYKHSKYSVGISIPLIQRKASVVSSGGDYTNSFVFNEGA	

aaSeqID 80 112	VLKFQKLPLLFVSILYNQSPLLAFDYKFSGVAESVSKVGFNHSKLNSKEGIFPTATFVT VSYDNTDDYYFPRNGVIFSSYATMSGLPSSGTLNS . * . * * . * . * *
80	TIKLOVDSNLLPKNIFKHSI VICUSOTT SALAM BLOCK B
112	TIKLQVDSNLLPKNIEKHSLKIGVGGILGALAYDSTKTLIDOATHQIYGSELFYLIGRWW NGLGGNVRNTKVYGKFAAYHHLQKYLLIDLIARFK * ** . * ** *
80	GFLGNA PWKDST, TESDA LIMBART - AREA
112	GFLGNAPWKDSLIESDAHTRNYVLYNSYLFYSYGDKFHLKLGRYLSNMDFMSSYTQGFEL TQGGYIFRYNTDDYLPLNSTFYMGGVTTVRGFRNG * * * * * * * * * * * * * * * * * *
80	DYKINSKIALYWESSESSESSESSESSESSESSESSESSESSESSESSESS
112	DYKINSKIALKWFSSFGRALAFGQWIRDWYAPIVTEDGRKEVYDGIHAAQLYFSKHVQV
	* ** *. * * ** *
80	MPFAYFSPKIYGAPGVKIHIDSNPKFKGLGLRAQTTINVIFPVYAKDLYDVYWRNSKIGE
112	BLOCK D
80	WGASLLIHORHDYNEFNEGECYYONEGY
112	WGASLLIHQREDYNEFNFGFGYYQNFGNANARIGWYGNPIPFNYRNNSVYGGVFSNAITAAPTTTANFHDYGVVGAGFERATWRASTGLQIEWISPMGPLVL
80	DAVSGYVFGGGVYRGFI WCTI CRYMYA
112	DAVSGYVFGGGVYRGFLWGILGRYTYATRASERSINLNLGYKWGSFARVDVNLEYYVVSMQWGD
	.**
80	HNGYRLDYLTGPFNKAFKADAQDRSNLMVSMKFFF
112	GNGKKCKGLCFNPNMNDYTQHFEFSMGTRF ** * * * * * *

FIGURE 7

MGCSFIFKKVRVYSKMLVALGLSSVLIGCAMNPSAETKKPNDAKNQQPVQTHERMTTSSE --EVALKLNYHPASE HVTPLDFNYPVHIVQAPQNHH\VGILMPRIQVSDN-LKPYIDKFQDALINQIQTIFEKRG ILLLRPAFQYSDNIAKEYENKFK\\QTTLKVEEILQNQG YQVLRFQ--DEKALNVQ\KKKIFSVLDLKGWVGILEDLKMNLKDPNSP\-NLDTLVDQSS **YKVINVDSSDKDDFSFA**¶KKEGYLAVAMNGEIVLRPDPKRTIQKKSEP|3LLFSTGLDKME GSVWFNFYEPESNRVVHDFAVEVBTFQAITYTYTSTNNASGGFNSSKSVIHENL RVLIPAGEVKVTILEPMSGESLDSFTMDLBELDIQEKFLKTTHSSHSGG--LVSTMVKGT DKNREDAIHKILNRMYAVVMKKAVTI|LTKENIAKYRDAIDRMKGFK|SSMPQKK D-NSNDAIKSALNKIFASIMQEMDKHLTQRNLESYQKDAKELKNKRNR----BLOCK E MKTNGHFKDF-AWKKCFLGASVVALLVGCSPHIIETN--BLOCK A BLOCK B BLOCK C BLOCK D KVQALDEKaa SeqID# 130 81 130 130 130 130 81 81 81 81

FIGURE 8

INTERNATIONAL SEARCH REPORT

International application No. PCT/US97/19575

4 6	AGGIRLO		
A. CL. IPC(6)	ASSIFICATION OF SUBJECT MATTER :A01N 43/04; A61K 31/70; C12Q 1/68		
US CL	:514/44; 435/6		
B. FIE	to International Patent Classification (IPC) or to	both national classification and IPC	
	documentation searched (classification system fo	llowed by classification and the	
U.S. :	514/44; 435/6	nowed by classification symbols)	
Documents GENEBA	ation searched other than minimum documentation	to the extent that such documents are included	d in the fields searched
Electronic NONE	data base consulted during the international search	ch (name of data base and, where practicable	e, search terms used)
C. DOC	CUMENTS CONSIDERED TO BE RELEVAN	т	
Category*	Citation of document, with indication, whe	re appropriate, of the relevant passages	Relevant to claim No.
A	TAYLOR, et al. Construction of a land Demonstration of Diversity at Bacteriology. November 1992, Vol. see entire document.	Helicobacter pylori Genome Map	1-65
A	AKOPYANZ, et al. DNA divers Helicobacter pylori detected by PO Nucleic Acids Research. 1992, Vol. see entire document.	R-based RAPD fingerprinting	1-65
Speci	r documents are listed in the continuation of Box al categories of cited documents: nent defining the general state of the art which is not considered of particular relevance	"T" later document published efter the intern	tion but cited to understand
earlier docum cited t	document published on or after the international filing date the state of any throw doubts on priority claim(s) or which is to establish the publication date of another citation or other treason (as specified)	"X" document of particular relevance, the considered novel or cannot be considered when the document is taken alone	isimed invention cannot be to involve an inventive step
docum means	ent referring to an oral disclosure, use, exhibition or other	"Y" document of particular relevance, the c considered to involve an inventive sit combined with one or more other such debeing obvious to a person skilled in the	ep when the document is
	ent published prior to the international filing date but later than ority date claimed	*&* document member of the same patent far	
e of the act	ual completion of the international search	Date of mailing of the international searc	h report
7 FEBRUAI	RY 1998	1 3 MAR 1998	
ox PCT	ing address of the ISA/US of Patents and Trademarks	Authorized officer	
ashington, D.		GINNY PORTNER ! MIN	W
simile No.	(703) 305-3230	Telephone No. (703) 308-0196	

Form PCT/ISA/210 (second sheet)(July 1992) *

INTERNATIONAL SEARCH REPORT

International application No. PCT/US97/19575

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
Please See Extra Sheet.
1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. X As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: 1-65, SEQ. ID Nos. 1, 7, 8, 11, 37, 39, 43, 45, 55, 61, 74, 80, 81 and 112
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest.
X No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet(1))(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No. PCT/US97/19575

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-26, 47, 49, 51, 53, 55, 57, 59, and 61, drawn to no fewer than 135 nucleic acid molecules, vectors containing the nucleic acid molecules, DNA encoding fragments of the polypeptides encoded by the no fewer than 135 different DNAs, organism transformed with the nucleic acid molecules, vaccines and methods of producing polypeptides encoded by the no fewer than 135 different nucleic acid molecules.

Group II, claim(s) 27-46, 48, 50, 52, 54, 56, 58, 60, and 62-65 are, drawn to no fewer than 73 polypeptides encoded by a subset of the encoding DNA mentioned in Group I.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

Group I contains a separate DNA species for each sequence mentioned. Therefore, there is a minimum of 135 species.

Group II contains at least one polypeptide for each DNA sequence mentioned. Therefore, this is a minimum of 73 species in Group II.

For either Group that applicant elects, a total of 10 (ten) specified sequences will be searched and no more than 4 (four) specified sequences will be searched for each additional fee paid; if no additional fee is paid and no election indicated the first 10 sequences appearing in Group I will be searched.

and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I and II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The polypeptide encoding DNAs, vectors containing them, organisms transformed with them and methods of polypeptide production using them of Group I are materially different from each other and are therefore independent from the polypeptides of Group II. Additionally, none of the products or methods of Group I is needed to make the polypeptides of Group II.

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: There is no relationship between or among the various nucleotide and amino acid sequences mentioned in the claims.

Form PCT/ISA/210 (extra sheet)(July 1992) *